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08/619,649	03/27/1996	RADOJE DRMANAC	ARCD:146/BOW	7575

<sup>7590</sup>  
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EXAMINER
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FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

MAIL DATE	DELIVERY MODE
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11/12/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

08/619,649

**Applicant(s)**

DRMANAC, RADOJE

**Examiner**

BJ Forman

**Art Unit**

1634

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 October 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 97, 157-175, 177-182 and 184-188 is/are pending in the application.
- 4a) Of the above claim(s) 176 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 97, 157-175, 177-182 and 184-188 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**FINAL ACTION**

***Status of the Claims***

1. This action is in response to papers filed 12 October 2010 in which the previous rejections were traversed and claims 183 and 189 were canceled

It is noted that Claims 97 and 166 have been amended to delete amendments filed 7 October 2010. Currently pending claims 97 and 166 are thus identical to the previously examined claims.

The previous rejections in the Office Action dated 7 April 2010 under 35 U.S.C. 112, first paragraph are withdrawn in view of the canceled claims.

The previous rejections under 35 U.S.C. 103(a) are maintained.

Applicant's arguments have been thoroughly reviewed and are discussed below.

Claims 97, 157-175, 177-182 and 184-188 are under prosecution.

***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 97, 157-175, 177-182, 184, 186-187 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (Genomics, 1992, 13: 1008-1017) in view of

Kauvar (U.S. Patent No. 5,356,784, issued 18 October 1994) and/or Wang (U.S. Patent No. 4,618,475, issued 21 October 1986).

Regarding Claims 97, 157-158, 166-168, 177-182 and 186, Southern discloses a support comprising an array of four microchips, each having an array of oligonucleotide probes immobilized thereon (Fig. 3, figure legend, line 1). Southern teaches each array is in one of four quadrants on the surface (Fig. 3). The four-quadrant arrangement is encompassed by the physical separation because a quadrant defines a physical location of the surface. Assignment of an array to a quadrant defines a boundary between quadrants, the boundary being the point of physical separation. The reference specifically teaches that the arrays are physically separated, Southern does not specifically teach a physical barrier for keeping the arrays and/or probes in corresponding arrays. However, physical barriers grooved and/or hydrophobic were well known in the hybridization art at the time the invention was made as taught by Kauvar and Wang.

Kauvar teaches an array of reaction regions on a solid support, each region having a plurality of ligands immobilized in the region wherein the regions are separated by a hydrophobic barriers (Column 7, lines 39-45) whereby reactions within the regions are defined thereby simplifying interpretation of assay results (Column 4, lines 37-58). Wang also teaches an array of reaction areas separated by hydrophobic barriers whereby cross-contamination is virtually eliminated and an "excellent appearance of the final product" is obtained (Column 4, lines 22-53).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the physical separation of Wang and/or Kauvar to the multiple arrays of Southern. One of ordinary skill in the art would have been motivated to do so, with a reasonable expectation of success, for the expected benefit obtaining clearly defined assay results as is well known and routinely practiced in the art of bio-assays (Kauvar, Column 4, lines 37-58 and Wang, Column 4, lines 22-53).

Regarding Claims 159 and 169, Southern discloses the support wherein the microchips are arranged in multiple rows and columns (i.e. two rows and two columns, Fig. 3). And Kauvar teaches the arrays in an orderly design pattern" (Column 4, line 60) and Wang teaches the similar support comprising multiple rows (Fig. 1).

Regarding Claims 160 and 170, Southern discloses the support wherein the microchips are positioned for use with a multichannel pipette (Fig. 3). The arrays of Southern are arranged in two rows of two columns. While Southern does not teach use of a multichannel pipette, the courts have stated that a claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. *Ex parte Masham*, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987). Southern teaches the structural elements of the claim and therefore, teaches the support of Claims 160 and 170.

Regarding Claim 161 and 171, Kauvar teaches the apparatus is used with labeled reagents and wash buffer (Column 5, line 55-Column 6, line 15). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was

made to combine the reagents used with the apparatus into a kit format for the well known benefits of kit convenience.

Regarding Claims 162 and 172, Southern teaches a 4 by 4 array but does not teach an 8 by 12 array. However, spotting probes in an 8 x 12 format (i.e. microtiter plate) was well known and routinely practiced in the art at the time the invention was made as taught by Kauvar who further teaches that any convenient or orderly pattern are chosen based on convenience (Column 4, lines 58-64).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the 8 by 12 format of Kauvar to the arrays of Southern based on desired format as taught by Kauvar (Column 4, lines 58-64).

Regarding Claims 163 and 173, Southern discloses the support wherein the array of microchips comprises more than 256 probes i.e. each of the four microchips has 256 probes. Hence, the support of Claim 97 has more than 256 probes per array as claimed.

Regarding Claims 164 and 174, Southern discloses the support wherein the probes are between 4 and 9 bases (Fig. 3).

Regarding Claims 165 and 175, Southern discloses the support wherein the probes are synthesized on the support (page 1009, left column). Southern does not teach light-directed synthesis. However, the courts have stated that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the

same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Because determination of patentability is based on the product and because Southern teaches the product, the process of making the product as recited in the claim does not define the product over that of Southern.

Regarding Claims 184 and 187, Southern teaches the support has duplicate arrays thereby providing arrays that are identical to other arrays, but different from others (Fig. 4 and accompanying text).

4. Claims 97, 157-175, 177-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac et al (Electrophoresis, 1992, 13:566-573) in view of Kauvar (U.S. Patent No. 5,356,784, issued 18 October 1994) and/or Wang (U.S. Patent No. 4,618,475, issued 21 October 1986).

Regarding Claims 97, 157-158, 166-168, 177-182 and 186 Drmanac discloses a support comprising multiple microarrays (Fig. 4), each comprising an array of differing oligonucleotides immobilized thereon wherein the microarrays are separated from each other. The arrays illustrated in Fig. 4 clearly appear to be separated by a barrier, and the reference teaches that hybridization with different samples requires separation (page 571, last paragraph). The reference does not specifically teach physical barriers for keeping the arrays and/or probes in corresponding arrays. However, physical

barriers grooved and/or hydrophobic were well known in the hybridization art at the time the invention was made as taught by Kauvar and Wang.

Kauvar teaches an array of reaction regions on a solid support, each region having a plurality of ligands immobilized in the region wherein the regions are separated by a hydrophobic barriers (Column 7, lines 39-45) whereby reactions within the regions are defined thereby simplifying interpretation of assay results (Column 4, lines 37-58). Wang also teaches an array of reaction areas separated by hydrophobic barriers whereby cross-contamination is virtually eliminated and an "excellent appearance of the final product" is obtained (Column 4, lines 22-53).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the physical separation of Wang and/or Kauvar to the multiple arrays of Drmanac. One of ordinary skill in the art would have been motivated to do so, with a reasonable expectation of success, for the expected benefit obtaining clearly defined assay results as is well known and routinely practiced in the art of bio-assays (Kauvar, Column 4, lines 37-58 and Wang, Column 4, lines 22-53).

Regarding Claims 159 and 169, Drmanac teaches the support wherein the microchips are arranged in multiple rows and columns (Fig. 4). And Kauvar teaches the arrays in an orderly design pattern" (Column 4, line 60) and Wang teaches the similar support comprising multiple rows (Fig. 1).

Regarding Claims 160,170, 183 and 189 Drmanac teaches the support wherein the microchips are "positioned" for use with a multichannel pipette (i.e. arrayed, Fig. 4).



Regarding Claim 161 and 171, Drmanac teaches hybridization reagents (page 571). Hardy teaches the similar support and hybridization reagents (Column 11).

Regarding Claims 162 and 172, Drmanac teaches the arrays are arrayed in 8 by 12 format (paragraph spanning pages 569-570).

Regarding Claims 163 and 173, Drmanac teaches the support wherein the array of microchips comprises more than 256 probes (page 569-570).

Regarding Claims 164 and 174, Drmanac teaches the support wherein the probes of between 4 and 9 bases are spotted onto the arrays for hybridization (page 571).

Regarding Claims 165 and 175, Drmanac teaches the support of Claims 97 and 166 as discussed above. While the reference does not teach light-directed synthesis. However, the courts have stated that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Because determination of patentability is based on the product and because the combination of Drmanac and Hardy teach the product, the process of making the product as recited in the claim does not define the product over the prior art.

Regarding Claims 184-185 and 187-188, Drmanac teaches the support has duplicate arrays thereby providing arrays that are identical to other arrays, but different from others (Fig. 4 and accompanying text).

### ***Response to Arguments***

5. Applicant acknowledges that Kauvar teaches assay regions separated by physical barriers, but asserts that the reference does not render obvious the instantly claimed invention because Kauvar is only interested in measuring a single analyte. Applicant argues that this contrasts with the instantly claimed invention that is intended to identify or bind different analytes.

The argument has been considered but is not found convincing. First, the claims do not define identification or binding of different analytes. Therefore, the argument is not commensurate in scope with the claims. Second, while Claims 97 and 166 define oligonucleotides having different sequences, Claims 181-182, 184-188 are not so limited. Therefore, the argument is not relevant to any use of Claims 181-182, 184-188. Finally, the fact that Kauvar only teaches a single analyte does not alter the fact that the reference is clearly and specifically interested in obtaining assay region-signals and to do so provides barriers between the assay regions for "convenience and simplicity of interpreting results" (Column 4, lines 53-55).

Applicant further argues that Southern's arrangement of four arrays provides parallel use of the arrays in the same hybridization reaction but not different probes for use in individual arrays. Applicant argues that one of ordinary skill would not be

motivated to combine the teaching of Southern and Kauvar because the references are interested in different endeavors i.e. Southern is interested in sequencing and Kauvar is interested in analyte detection.

The argument has been considered but is not found persuasive because both Southern and Kauvar are interested in detecting region-specific signals. Southern specifically teaches "[T]o quantify the intensity in each cell, a grid was superimposed over the array so that each spot lay at approximately the center of the grid" (lines 8-9 of figure legend for Fig. 3). Kauvar is also interested in region-specific signal detection "convenience and simplicity of interpreting results" (Column 4, lines 53-55). Hence, Southern and Kauvar have a common goal of detecting region-specific signals. It is maintained that the combination of Southern and Kauvar is reasonable and that adding the barriers of Kauvar to the arrays of Southern would have been an obvious modification at the time of the instant invention.

Applicant argues that the combination of Southern and Wang does not render the invention obvious because Wang does not teach why it would be desirable or necessary to place their hydrophobic material between the four arrays of Southern. Applicant asserts that absent a teaching in Southern or Wang that modification of Southern would be required, the skilled artisan would not have been motivated to do so.

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so

found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, as stated in the rejection, Wang clearly teaches the advantages of providing barriers to separate assay regions. It is maintained that it would have been obvious to apply the separating barriers of Wang to the substrate of Southern to prevent cross-contamination between assay regions and obtain assay region-specific detection as desired by Southern.

Applicant further argues that the examiner applied hindsight reasoning to construct the rejection.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Furthermore, given the multiple arrays of Southern it would have obvious to one of ordinary skill to apply the barriers of Kauvar and/or Wang to thereby extend the usefulness of Southern's multiple arrays. Based on the teaching of Kauvar and/or

Wang the artisan would have recognized that adding barriers to Southern's arrays would have allowed differential assays along with Southern's desired differential detection thereby extending the usefulness of the multiple arrays. It is maintained that the combination of Southern and Kauvar and/or Wang is reasonable and that adding the prior art barriers to the arrays of Southern would have been obvious to one of ordinary skill at the time of the instant invention.

Regarding the rejection over Drmanac in view of Kauvar and Wang, Applicant argues that Drmanac does not immobilize the probes and therefore separation of the different areas is not critical and because separation is not critical, there would be no reason to provide the areas with the barriers of Kauvar and/or Wang. Applicant further argues that one of ordinary skill would not be motivated to combine the teaching of Drmanac and Kauvar and/or Wang because the references are interested in different endeavors i.e. Drmanac is interested in target identification and Kauvar is interested in increased sensitivity of analyte detection.

The argument has been considered but is not found persuasive because both Drmanac, Kauvar and Wang are all interested in detecting region-specific signals based on analyte binding. Hence, Southern, Kauvar and Wang have a common goal of detecting region-specific signals. Furthermore, it would have obvious to one of ordinary skill to apply the barriers of Kauvar and/or Wang to the multiple arrays of Drmanac thereby extend the usefulness of Drmanac's multiple arrays. Based on the teaching of Kauvar and/or Wang the artisan would have recognized that adding barriers to Drmanac's arrays would have allowed differential assays in addition to region-specific

detection thereby extending the usefulness of the multiple arrays. It is maintained that the combination of Drmanac and Kauvar and/or Wang is reasonable and that adding the barriers of Kauvar and/or Wang to the arrays of Drmanac would have been an obvious modification at the time of the instant invention.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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